D3

vasconstrictors, chermotherapeutic drugs, antibiotics, keratolytics, cauterizing agents, or antiviral drugs.

Remarks

A marked-up version of claims 1, 3 and 13 showing the changes made to the claims are attached hereto.

Favorable reconsideration in view of the herewith presented amendment and remarks is respectfully requested.

The typographical error noted by the Examiner in claim 13 has been corrected.

Claims 1, 3 9 and 11 to 13 have been rejected under 35 USC §112, second paragraphs, as allegedly being indefinite.

Claims 3 and 13 have been amended in a manner which is believed to address the Examiner's technical objections.

As for the objection to claim 1, applicants believe that the Examiner's viewpoint is in error. The claims must be read from the viewpoint of one skilled in the pertinent art area. It is respectfully urged that the ordinary artisan having the benefit of claim 1 and the supporting disclosure as well as the requisite knowledge of the ordinary artisan would be apprised of the scope and content of claim 1.

The instant disclosure includes at pages 2 and 3 a discussion of hemostasis and clot formation. The blood coagulation cascade is discussed as in wound healing and thrombia. Fibrinogen is discussed on pages 5 and 6. The cascade-like effect initiated by the hemostatic polymers used in the instant invention is discussed at page 11. The term "other ancillary substances" is not used alone but with the clause "...which initiate the physiological clotting process....".

Applicants urge that the artisan having the requisite knowledge of the art area as well as the present disclosure would not be confused by what was encompassed by the recitation in claim 1 alleged to be objectionable by the Examiner.

Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 3, 9 12 and 13 have been rejected under 35 USCD §102 as allegedly being anticipated by GB 1,454,055 (UK 055).

Claim 11 has been rejected under 35 USC §103(a) as allegedly being unpatentable over UK 055 further in view of Larson, or Eloy et al and Wang.

Applicants respectfully traverse both of these rejections.

The present invention relates to use of a hemostatic agent or polymer composition comprising beads of cross-linked dextran which cause a cascade-like effect and the rapid induction of blood coagulation and hemostasis at an active bleeding site. The beads absorb water, low molecular weight (MW) blood and plasma constituents into the grains or beads, while high MW constituents such as fibrinogen, platelets, and clotting factors are concentrated on the surface of the grains or beads and the bleeding site. This concentration results in rapid blood coagulation and hemostasis without the use of extraneous or other exogenous compounds. Instant claim 1 specifies the molecular weight exclusion of the cross-linked dextran and that the nature of the beads is such that the beads induce a physiological clotting process at a bleeding site. The instant claims are limited in a way such that cross-linked dextran beads which do not induce clotting at a bleeding are excluded from the claims.

The Sephadex that is the basis of UK 055 patent is Sephadex G-25 (MS Exclusion limit: 5,000 and water regain 2.5 ml/gm. Sephadex G-50 (MS Exclusion limit: 30,000 and water regain 5.0 ml/gm) will act somewhat similar to the G-25 but the G-25 clearly makes a clot that is well adhered to the tissue at the site of bleeding.

The main issue with MW range of the cross-linked dextrans used in the present invention is that they all have a relatively high rate of water regain compared to the preferred embodiment of the UK 055 patent. The preferred embodiment of the invention would be the G-150 with a water regain of 15 ml/gm of dry polymer. The preferred embodiment of the UK 055 is G-25 with a water regain of only 2.5 ml/gm of dry polymer. At the lower level of water regain you do not form a clot like material in blood but more of a loosely associated gel. However, with the higher rate of water regain associated with G-150, you get a very well formed clot like material that is adherent to the underlying tissue. This is due to the concentrating effect on the active coagulation factors as described in the present patent application. This process does not take place in the UK 055 patent because they state on page 3, line 96, that "The particles should normally absorb water and swell at a rate which is sufficiently high that fibrin and fibrin coagulum, cannot be formed by the influence of the enzyme thrombin etc. in the zone adjacent the discharging surface." The difference with the preferred embodiment in the present application is that just the opposite occurs and that is the rate is sufficiently high enough to produce a rapid concentration of the clotting factors including fibrin and thrombin at the site of bleeding and thus forming a durable clot like material which is adherent to the bleeding tissue.

A second factor besides water absorption is that the molecular weight range of polymers used in the invention all absorb the potent anticoagulant substance present in plasma because they have molecular weights less than 100,000. Thus in a preferred embodiment of the UK 055 with a molecular cut of 5000, these anticoagulant substance are concentrated on the outside of the polymer along with the coagulation factors and thus inhibit the formation of a clot like substance which is what is required if the resulting gel is to be easily washed off the tissue. The anticoagulant substance include the following:

1) Heparin (a sulphated glycosaminoglycan), plasma concentration of 30-800 ng/ml, MW 5000 to 30,000.

2) Heparin Cofactor II (HCII), plasma concentration of 0.5 to 1.4 μg/ml, MW 58,000.

3) Antithrombin III (ATIII), plasma concentration of 125 μg/ml, MW 58,000.

4) Tissue Factor Pathway Inhibitor (TFPI), plasma concentration of 100 ng/ml, MW 43,000.

5) C1 Esterase Inhibitor (C1INH), plasma concentration of 100 μg/ml, MW 104,000.

6) Protein C, plasma concentration of 4 μg/ml, MW 21,000.

7) Protein S, plasma concentration of 20 to 25 μg/ml, MW 69,000.

Low molecular weight cut off polymers such as G-25 would concentrate all of these substances along with the essential clotting factor and thus act to inhibit coagulation. Once the molecular weight cut off is high enough to allow these

anticoagulant substance to enter the polymer, then their concentration would be rapidly reduced in the material on the surface of the polymer and partitioned away from the coagulation factors. Thus the combination of rapid removal of water and partitioning of lower molecular weight anticoagulant surface away from the higher molecular weight clotting factors such as thrombin and fibrin creates the proper environment for the formation of a adherent clot at the site of active bleeding.

It is urged that the UK 055 does not direct the artisan to the physical characteristics of the polymers that stop bleeding and adhere to the bleeding tissue to form a clot in comparison to the polymers that act as a wound cleaning system, moving fluid and protein away from the site of exudation. UK 055 does not provide an enabling disclosure from which the artisan could have made or used the instant invention. As previously noted, UK 055 actually leads away from the invention by requiring that clotting is not occurring at the surface of the wound.

For the above reasons, applicants urge that UK 055 fails as a proper anticipation of the present claims. The secondary reference relied upon by the Examiner fail to remedy the deficiencies of UK 055.

Reconsideration and withdrawal of the §102 and §103(a) rejections is respectfully requested.

It is believed that the present claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited.

AUTHORIZATION

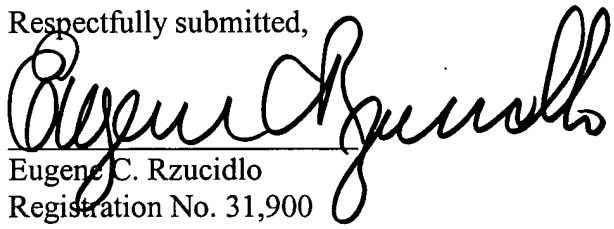
If the Examiner believes that issues may be resolved by telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2146. The undersigned may also be contacted by e-mail at ecr@gtlaw.com.

No additional fee is believed to be necessary. The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 50-1561.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-1561.

Respectfully submitted,

Dated: December 23, 2002

By: 

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ATTACHMENT

1. (Amended) A dry, storage stable, sterile dressing for application to a bleeding site which comprises a dry hemostatic zone, said zone comprising a matrix containing hemostatis-promoting amount of a hemostatic agent which accelerates blood coagulation and clot formation at an interface between the bleeding site and the hemostatic zone wherein said hemostatic agent comprises beads of cross-linked dextran wherein said cross-linked dextran has a molecular weight exclusion limit of 100,000 to 650,000 and triggers release of clotting factors and other ancillary substances which initiate a physiological clotting process when applied to the bleeding site.

3. (Amended) The dry, sterile, dressing according to claim 1 wherein the [dressing] hemostatic zone is affixed to a substrate.

13. (Amended) The dressing according to claim 12, wherein said pharmaceutical agent is at least one of anti-inflammatory analgesic agents, steroidal anti-inflammatory agents, antihistamines, local anesthetics, bactericides or disinfectants, vasconstrictors, chermotherapeutic drugs, antibiotics, keratolytics, cauterizing agents, or antiviral drugs [antivirual drugs and mixtures thereof].